Journal of Molecular Liquids 220 (2016) 324–328

Contents lists available at ScienceDirect

Journal of Molecular Liquids

journal homepage: www.elsevier.com/locate/molliq

One-pot synthesis of quinoline derivatives using choline chloride/tin (II) chloride deep eutectic solvent as a green catalyst

Dana Shahabi, Hossein Tavakol *

Department of Chemistry, Isfahan University of Technology, Isfahan 84156-83111, Iran

ARTICLE INFO

Article history:
Received 28 November 2015
Accepted 22 April 2016
Available online xxxx

Keywords:
Catalyst
Deep eutectic solvent
Multi-component
Quinolines

ABSTRACT

In this work, various quinoline derivatives were prepared efficiently through a one-pot, three component synthesis using choline chloride/tin(II) chloride ($ChCl \cdot 2SnCl_2$) deep eutectic solvent (DES) as a green catalyst. The procedure is free of using toxic solvents or catalyst and it could be categorized as a green method. In this procedure, aniline derivatives, aromatic aldehydes and enolizable aldehydes were mixed in the presence of DES that plays both roles of solvent and the reaction catalyst. Using this methodology, quinoline derivatives were synthesized simply at 60 °C in 2–3 h with high yields (54–97%). All products were purified by chromatography and recrystallization in ethanol. The employed DES have been recycled 4 time without important loss of its activity.

1. Introduction

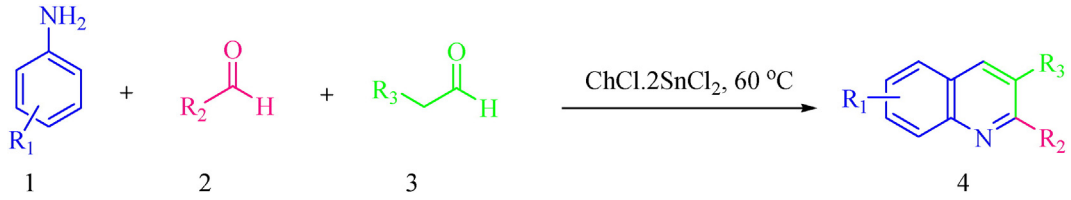
Quinoline (and its derivatives) is one of the most important nitrogen-containing heterocyclic aromatic compounds because of its biological activities [1–6]. Although, quinoline derivatives have shown antiviral [7], antimalarial [8–10], antibacterial [11–13], anticancer [14], antifungals [15], anti-inflammatory and antihypertensive [16,17] activities. Quinolines are well known not only for their significant biological activities, but also because of their applications in the formation of conjugated molecules and polymers [18]. These materials combined enhanced electronic, optoelectronic, or nonlinear optical properties with excellent mechanical properties [19–21]. Quinoline derivatives have been used in the synthesis of fungicides, biocides and flavoring agents [22,23]. Furthermore, these compounds are useful in chemistry of transition metal catalysts, uniform polymerization and luminescence chemistry [24,25], in addition to their applications as antifoaming agent in refineries [26]. Therefore, quinoline derivatives have been attracted much attention because of their broad range of activities and wide applications.

The main sources of quinoline are petroleum, coal processing, wood preservation and shale oil. The quinoline derivatives could be observed in various natural products. In this line, several quinoline derivatives have been isolated from natural resources or prepared synthetically. In 1820, quinine (a derivative of quinoline) was isolated from the bark of the *cinchona tree* and it has been used in the treatment of malaria for many years. After this discovery, many quinoline derivatives have been isolated from different plants and used in various applications [27]. In addition, quinoline was extracted from the coal tar in 1834 and during these years, coal tar has been remained as a major source of commercial quinoline [28]. However, because of the limitations in the use of natural resources, the syntheses of quinolines have been the subject of great focus in by synthetic organic chemists.

The first synthesis of quinoline was reported by Skraup over a century ago. After the Skraup synthesis, many synthetic methods such as Doebner-Von Miller, Friedlander [29] and Combes reactions have been developed for the preparation of quinolines. In addition, many catalysts have been used involving a variety of metal catalysts and Lewis acids. However, many of these procedures are not fully acceptable because of some problems in their operational simplicity, cost and toxicity of the reagents, reaction time and isolated yields. Thus, it is necessary to find new methodologies for the synthesis of quinolines. More importantly, the main disadvantage of the most of reported methods is the poor recoverability of the employed catalyst and in the cases where the catalyst could be recovered, the preparation of the catalyst needs to hazardous or expensive materials and hard procedures [30–34]. Therefore, presenting a simple synthesis of quinolines that involves economic and environmental friendly chemical processes could be useful. In this line, in continuation of our interests on the use of deep eutectic solvents (DESs) as a green media in organic synthesis [35,36] the attempts have been made for the syntheses of quinolines using DES (also known as deep eutectic ionic liquids (DEILs)), low-melting mixtures (LMMs) or low transition temperature mixtures (LTTMs). DESs are a green class of common organic solvents that mostly avoid their problems such as high flammability, volatility, hazardness, and toxicity. During last decades, the search for environmentally-friend substitutes for organic solvents has recently gained more attention in green chemistry. DESs have become more and more attractive in recent years due to their interesting properties and benefits, such as low cost of components, easy to prepare, tunable physicochemical properties, negligible

* Corresponding author.
E-mail addresses: H_tavakol@cc.iut.ac.ir, h_tavakol@yahoo.com (H. Tavakol).

http://dx.doi.org/10.1016/j.molliq.2016.04.094
0167-7322/



Scheme 1. The general reaction for the synthesis of quinoline derivatives in presence of DES.

vapor pressure, non-toxicity, non-reactivity with water, non-flammability, conductivity, bio renewability and biodegradability [37, 38]. In addition, when they are consisted of common catalyst (such as Lewis acid or base), they could play a role of catalyst, in addition to their solvent role. These DESs have been widely used as green and sustainable media as well as catalysts in many chemical processes.

In this study, we wish to report a new, simple and efficient method for the synthesis of quinoline derivatives from aniline, aromatic aldehydes and enolizable aldehydes in presence of choline chloride/tin(II) chloride DES as an efficient media. Moreover, the catalytic recoverability of the DES were investigated to show its high potency. The results obtained in this work and the employed methodologies will be discussed in the next sections.

2. Experimental

Chemicals were purchased from Merck and Sigma-Aldrich companies. Progress of the reactions was followed by thin layer chromatography (TLC) using silica gel 60 PF_{254} plates. Melting points were measured in capillary tubes using Gallen Kamp melting point instrument without correction. IR spectra were recorded with KBr pellets on JASCO FT-IR spectrophotometers in the range of 400 to 4000 cm^{-1}. ^1H and ^{13}C NMR (respectively in 400 and 125 MHz) spectra were recorded on a Bruker Ultrashield 400 MHz spectrometer in $CDCl_3$ solution. ^1H and ^{13}C chemical shifts are referenced to TMS as an internal standard.

2.1. Preparation of DES

A mixture of choline chloride/tin(II) chloride with 1:2 ratio was heated with stirring until a clear colorless liquid was obtained. The mixture was used without further purification.

2.2. General procedure for the synthesis of quinoline derivatives

Aniline derivative (1 mmol), aromatic aldehyde (1 mmol), enolizable aldehyde (1 mmol) and $ChCl{\cdot}2SnCl_2$ (5 mol%) was mixed in a 25 mL round-bottom flask equipped with a condenser on the top. The reaction mixture has been stirred for 2–3 h and during stirring, it was warmed slowly on the oil bath to 60 °C. The progress of the reaction was monitored by TLC (eluent phase = n-hexane: EtOAc = 3:1). After completion of the reaction, the mixture was diluted with water (5 mL) and Et_2O (2 × 5 mL) and shaken vigorously. The organic layer was separated from the aqueous layer (consisted of DES) by simple liquid-liquid extraction. The deep eutectic solvent was dried at 60–70 °C to remove water and reused. The organic layer was dried over $MgSO_4$ and its solvent was evaporated. The crude product was recrystallized in ethanol to give the pure product or purified by column chromatography over silica gel (hexane: ethyl acetate ratio: 3:1). All products were known compounds and their physical and spectroscopic data (mp, IR, ^1H NMR, ^{13}C NMR) were compared with those of authentic samples in the references [39–46]. The physical and spectroscopic data for selected compounds are as follows.

Quinoline: Pale yellow oil, FT-IR (KBr): ν_{max} = 3057, 3035, 1595, 1570, 1550, 1534, 1500, 868, 805, 786, 759, 738 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.09 (t, 1H), 7.35 (t, 1H), 7.58 (m, 2H), 7.82 (d, 1H), 8.32 (d, 1H), 8.94 (d, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 120.2, 125.5, 127.0, 127.4, 128.5, 128.6, 134.9, 147.5, 149.5 ppm.

1-phenyl-2-(quinolin-2(1H)-ylidene) ethanone (the tautomer form of the expected quinoline derivative): Pale yellow solid, mp = 108–110 °C, FT-IR (KBr): ν_{max} = 3428, 3059, 1628, 1580, 1549, 849, 824, 797, 752, 727, 690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.06 (s, 1H), 6.79 (d, 1H), 7.02 (t, 1H), 7.45 (m, 4H), 7.49 (m, 2H), 7.56 (d, 1H), 7.96 (m, 2H), 15.69 (bs, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 89.9, 118.1, 122.3, 123.3, 123.7, 126.7, 127.6, 128.3, 130.4, 131.0, 136.2, 137.8, 139.8, 154.1, 183.9 ppm.

3. Results and discussion

Initially, we chose the model reaction between aniline (1 mmol), benzaldehyde (1 mmol) and acetaldehyde (1 mmol) in the presence of DES to optimize the reaction parameters and obtain the best conditions for the general reaction according to Scheme 1. Different reaction conditions such as the amount of DES (5, 10 and 20 mol%), reaction temperature (r.t, 40, 60, 80 °C) and the reaction time (0.5, 1, 2, 5 h) were changed and the preparation of product was monitored. The results were listed in Table 1 that showed the best yield of the product could be obtained by carrying out the reaction at 60 °C in the presence of 5 mol% of catalyst at 2 h (Table 1, entry 8). Therefore, we employed these conditions to prepare other derivatives of quinoline according to the general reaction (Scheme 1) but in preparation of some derivatives, the time was increased to 3 h to improve the yield of the reaction.

The details of all prepared quinolines and obtained products were shown in Table 2. In one especial case (entry 16 of the table), instead of quinoline derivatives, its tautomeric form was obtained. According to this table, a variety of arylaldehydes containing electron-withdrawing and electron-donating groups at the ortho, meta or para position were used.

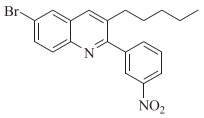
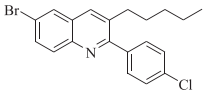
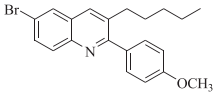
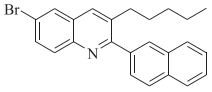
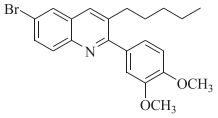
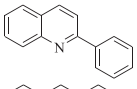
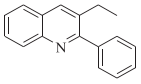
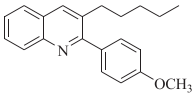
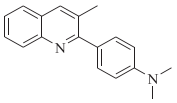
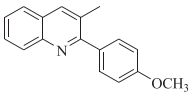
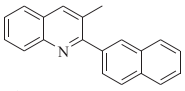
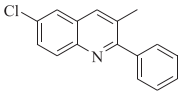
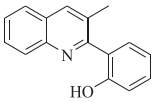
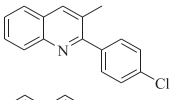
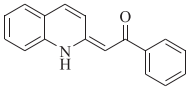
In addition, aniline and its 4-chloro and 4-bromo derivatives were used as aromatic amine source, in attendant with various enolizable aldehydes (ethanal, propanal, butanal and heptanal) to show the versatility of the reaction. It is important to note that some of the optimization reactions were also carried out without the presence of DES as a catalyst and solvent (Table 1, entries 1–4). Under these conditions, the desired

Table 1
Optimization of Reaction Conditions for the Synthesis of the model reaction[a].

Entry	Catalyst	T (°C)	Cat (Mol %)	Time (h)	Yield (%)[b]
1	$ChCl{\cdot}2SnCl_2$	r.t.	20	5	0
2	$ChCl{\cdot}2SnCl_2$	40	20	5	30
3	$ChCl{\cdot}2SnCl_2$	60	20	5	94
4	$ChCl{\cdot}2SnCl_2$	80	20	5	90
5	$ChCl{\cdot}2SnCl_2$	60	10	5	96
6	$ChCl{\cdot}2SnCl_2$	60	5	5	96
7	$ChCl{\cdot}2SnCl_2$	60	5	2	96
8	$ChCl{\cdot}2SnCl_2$	60	5	1	62
9	$ChCl{\cdot}2SnCl_2$	60	5	30 min	45
10	$ChCl{\cdot}2ZnCl_2$	60	5	2	73
11	ChCl·2Urea	60	5	2	10

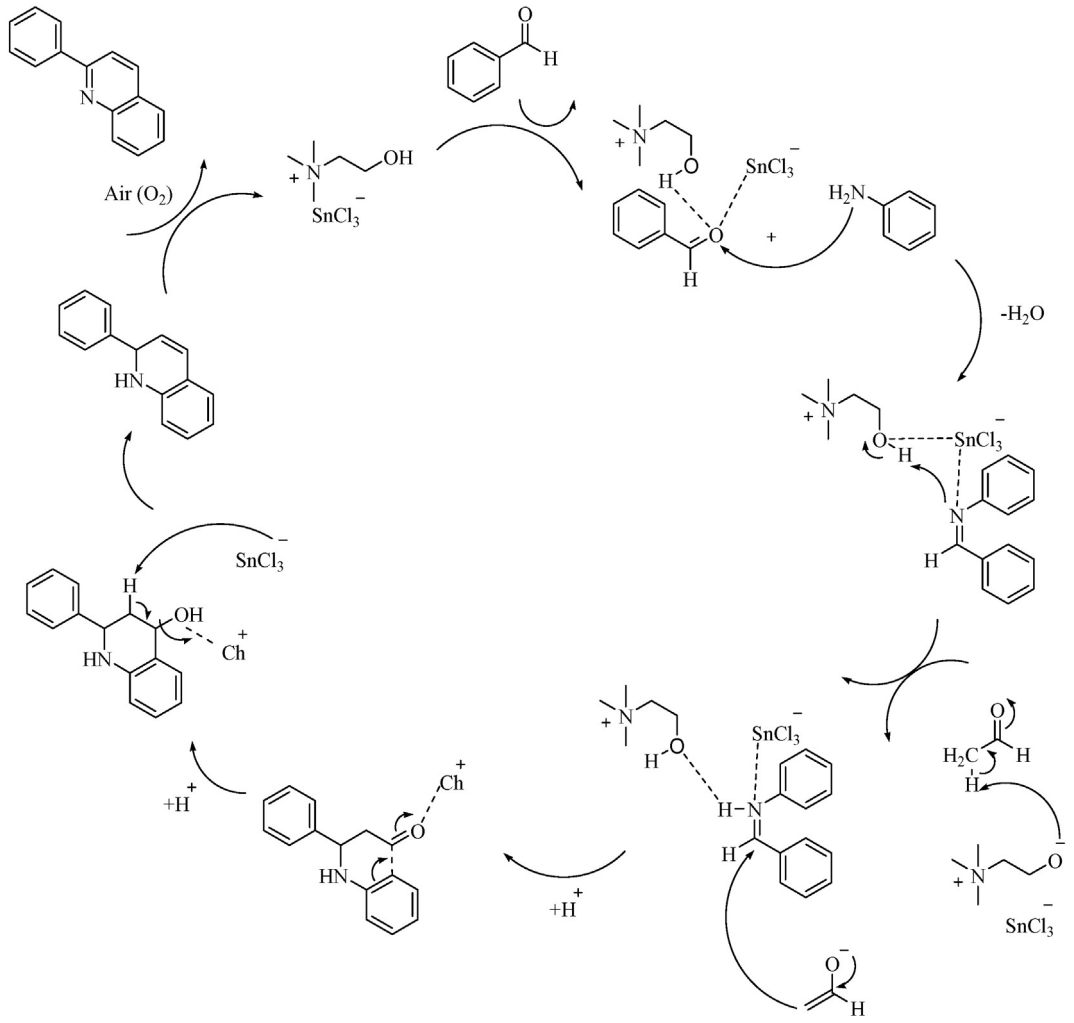
[a] The model reaction: aniline (1 mmol), benzaldehyde (1 mmol) and acetaldehyde (1 mmol).
[b] Isolated yield.

Table 2
One-pot, three-component synthesis of quinoline derivatives catalyzed by $ChCl{\cdot}2SnCl_2$[a].

Entry	R_1	R_2	R_3	Product	Time (h)	Yield(%)[b]	Mp	Ref
1	4-Br	3-NO_2-C_6H_4	C_5H_{11}		2	95	128–129	[39]
2	4-Br	4-Cl-C_6H_4	C_5H_{11}		3	96	102–104	[39]
3	4-Br	4-OCH_3-C_6H_4	C_5H_{11}		3	95	100–102	[39]
4	4-Br	Naphthyl	C_5H_{11}		2	72	110–112	[39]
5	4-Br	3,4-OCH_3-C_6H_4	C_5H_{11}		3	63	198–200	[39]
6	H	H	H		2	92	Oil	[39]
7	H	C_6H_5	H		2	96	Oil	[39]
8	H	C_6H_5	C_2H_5		2	93	Oil	[39]
9	H	4-OCH_3-C_6H_4	C_5H_{11}		2	54	Oil	[39]
10	H	4-$(Me)_2N$-C_6H_4	CH_3		2	97	100–102	[39]
11	H	4-OCH_3-C_6H_4	CH_3		3	87	104–106	[43]
12	H	Naphthyl	CH_3		4	64	109–111	[43]
13	4-Cl	C_6H_5	CH_3		2	76	104–107	[43]
14	H	2-OH-C_6H_4	CH_3		2	82	113–116	[44]
15	H	4-Cl-C_6H_4	CH_3		2	68	95–97	[45]
16	H	$CH_2COC_6H_4$	H		3	95	108–110	[46]

[a] Reaction conditions: a mixture of aniline derivatives (1 mmol), aryl aldehyde derivatives (1 mmol), aliphatic aldehyde derivatives (1 mmol) and DES (5mol%) were heated in an oil bath at 60 °C.
[b] Isolated yield.

quinolines were obtained between 0 and 71% yields. These results clearly show that the present DES catalyst is necessary for the synthesis of quinolines. By comparison between aniline and its derivatives and although between various enolizable aldehyde, any significant difference in their reactivities was not observed. However, aromatic aldehydes with electron withdrawing groups produced the products in the higher yields. To define the role of employed DES in the reaction, a reliable mechanism was proposed according to Scheme 2. The DES could be considered as choline cation and $SnCl_3$ anion that plays the both roles of Lewis acid (to activate the aldehyde or imine versus nucleophilic addition) and base (to get the proton of enolizable aldehyde and produce enolate anion).



Scheme 2. Proposed mechanism for the synthesis of quinolines catalyzed by $ChCl{\cdot}2SnCl_2$.

At the final step of this study, the reusability of DES, which is much important for industrial purposes and recommended for green processes [47,48], has also been explored in the model reaction. To test the reusability of the catalyst, after accomplishment of the reaction, the mixture was diluted with 5 mL of water and the organic phase was extracted using 2 × 5 mL of diethyl ether. The water of aqueous layer (consisted of DES) was evaporated to obtain the pure DES, it was dried at 60–70 °C and reused (for next three times) without further purification. All of these steps were performed quickly to avoid hydrolyzing tin chloride. The results were listed in Table 3 and they showed that the employed DES could be used at least four times without any significant loss in the yield of the product. It is more valuable when we know that simple $SnCl_2$ salt could be hydrolyzed in the excess values of the water. However, because of the nature of our DES and producing $SnCl_3^-$, it could be reused without hydrolyzing in the water.

Table 3
The reaction of benzaldehyde, aniline with acetaldehyde in DES.

Entry	Cycle	Time (hour)	Yield (%)
1	1st run	2	96
2	2nd run	2	94
3	3nd run	2	90
4	4nd run	2	88

4. Conclusion

In summary, we have developed an environmentally-friend and green approach for the synthesis of quinoline derivatives via a one-pot, multi-component reaction between aniline derivatives, aryl aldehydes and enolizable aldehydes in the presence of $ChCl_2{\cdot}SnCl_2$ DES as a green catalyst and solvent. This method offers several advantages including using of a green DES instead of toxic organic solvents or catalysts (or both), high yields, short reaction times, simple work-up procedure and reusability of DES.

Acknowledgement

The partial support of this work by the research council of Isfahan University of Technology is gratefully acknowledged.

References

[1] J. Elguero, In: Comprehensive Heterocyclic Chemistry. Vol. 5, Eds. A.R. Katritzky, C.W. Rees, K.T. Potts (Pergamon, Oxford, 1984) p. 167.
[2] R. Heusch, B. Leverkusen, Ullmann's Encyclopedia of Industrial Chemistry, 2000 (doi: 10.14356007: a09_297).
[3] G. Menozzi, L. Mosti, P. Fossa, F. Maltioli, M. Ghia, J. Heterocycl. Chem. 34 (1997) 963–968.
[4] U. Desai, S. Mitragotri, T. Thopate, D. Pore, P. Wadgaonkarb, ARKIVOC (2006) 198–204.
[5] E.E. Ebenso, M.M. Kabanda, T. Arslan, M. Saracoglu, F. Kandemirli, L.C. Murulana, A.K. Singh, S.K. Shukla, B. Hammouti, K. Khaled, Int. J. Electrochem. Sci. 7 (2012) 5643–5676.

[6] O.A. El-Sayed, F.B. El-Bieh, S.I. El-Aqeel, B.A. Al-Bassam, M.E. Hussein, Bull. Chim. Farm. 141 (2002) 461–465.
[7] P. Simrnoff, R.R. Crenshaw, Antimicrob. Agents Chemother. 11 (1997) 571–573.
[8] S. Bawa, S. Kumar, S. Drabu, R. Kumar, J. Pharm. Bio. Sci. 2 (2010) 64–71.
[9] A.A. Jashi, S.S. Narkhede, C.L. Viswanathan, Bioorg. Med. Chem. Lett. 15 (2005) 73–76.
[10] M. Ozyanik, S. Demirci, H. Bektas, N. Demirbas, A. Demirbas, S.A. Karaoglu, Turk. J. Chem. 36 (2012) 233–246.
[11] T. Suresh, R.N. Kumar, S. Magesh, P.S. Mohan, Indian J. Chem. 42B (2003) 2133–2135.
[12] T. Suresh, R.N. Kumar, S. Magesh, P.S. Mohan, Indian J. Chem. 42B (2003) 688–689.
[13] H.V. Patel, K.V. Vyas, P.S. Fernandes, Indian J. Chem. 29B (1990) 836–842.
[14] A. Dlugosz, D. Dus, Farmaco 51 (1996) 367–374.
[15] K. Majerz-Maniecka, B. Oleksyn, R. Musiol, B. Podeszwa, J. Polanski, Sci. Pharm. 73 (2005) 194.
[16] P.R. Graves, J.J. Kwiek, P. Fadden, R. Ray, K. Hardeman, A.M. Coley, M. Foley, T.A. Haystead, Mol. Pharmacol. 62 (2002) 1364–1372.
[17] Y.L. Chen, K.C. Fang, J.Y. Sheu, S.L. Hsu, C.C. Tzeng, J. Med. Chem. 44 (2001) 2374–2377.
[18] G.E. Tumambac, C.M. Rosencrance, C. Wolf, Tetrahedron 60 (2004) 11293–11297.
[19] S.A. Jenekhe, L. Lu, M.M. Alam, Macromolecules 34 (2001) 7315–7324.
[20] G. Jegou, S.A. Jenekhe, Macromolecules 34 (2001) 7926–7928.
[21] X. Zhang, A.S. Shetty, S.A. Jenekhe, Macromolecules 33 (2000) 2069–2082.
[22] G. Jones, In: Comprehensive Heterocyclic Chemistry II, Vol. 5 Eds. A.R. Katritzky, C.W. Rees, K.T. Potts (Pergamon, Oxford, 1984) pp 167.
[23] B.S. Holla, M. Mahalinga, M.S. Karthikeyan, P.M. Akberalib, N.S. Shettyc, Bioorg. Med. Chem. 14 (2006) 2040–2047.
[24] S. Całus, E. Gondek, A. Danel, B. Jarosz, M. Pokładko, A.V. Kityk, Mater. Lett. 61 (2007) 3292–3295.
[25] G. Caeiro, J.M. Lopes, P. Magnoux, P. Ayrault, F.R. Ribeiro, J. Catal. 249 (2007) 234–243.
[26] G. Caeiro, P. Magnoux, J.M. Lopes, F. Lemos, F.R. Ribeiro, J. Mol. Catal. A Chem. 249 (2006) 149–157.
[27] S. Gogoi, K. Shekarrao, A. Duarah, T.C. Bora, R.C. Boruah, Steroids 77 (2012) 1438–1445.
[28] R. Heusch, B. Leverkusen, Ullmann's Encyclopedia of Industrial Chemistry, John Wiley & Sons, NewYork, 2000 (2013).
[29] V.V. Kouznetsov, L.Y. Mendez, C.M. Gomez, Curr. Org. Chem. 9 (2005) 141–161.
[30] S. Ghassamipour, A.R. Sardarian, Tetrahedron Lett. (2009) 514–519.
[31] G.C. Muscia, M. Bollini, J.P. Carnevale, A.M. Bruno, S.E. Asis, Tetrahedron Lett. 47 (2006) 8811–8815.
[32] S.J. Song, S.J. Cho, D.K. Park, T.W. Kwan, S.A. Jenekhe, Tetrahedron Lett. 44 (2003) 255–257.
[33] M.A. Zolfigol, P. Salehi, M. Shiri, T. Faal-Rastegar, A. Ghaderi, J. Iran. Chem. Soc. 5 (2008) 490–497.
[34] S.S. Palimkar, S.A. Siddiqui, T. Daniel, R.J. Lahoti, K.V. Srinivasan, J. Org. Chem. 68 (2003) 9371–9378.
[35] F. Keshavarzipour, H. Tavakol, Catal. Lett. 145 (2015) 1062–1066.
[36] F. Keshavarzipour, H. Tavakol, J. Iran. Chem. Soc. (2015) doi: 101007/s13738-015-0722-9.
[37] J. Parnica, M. Antalik, J. Mol. Liq. 197 (2014) 23–26.
[38] A. Hayyan, F.S. Mjalli, I.M. AlNashef, Y.M. Al-Wahaibi, T. Al-Wahaibi, M.A. Hashim, J. Mol. Liq. 178 (2013) 137–141.
[39] S. Anvar, I. Mohammadpoor-Baltork, S. Tangestaninejad, M. Moghadam, V. Mirkhani, A.R. Khosropour, A. LandaraniIsfahani, R. Kia, Comb. Sci. 16 (2014) 93–100.
[40] M. Attimonelli, O. Sciacovelli, Org. Magn. Resonance. 12 (1979) 17–23.
[41] S.Y. Tanka, M. Yasuda, A. Baba, J. Org. Chem. 71 (2006) 800–803.
[42] J. Jacob, W.D. Jones, J. Org. Chem. 68 (2003) 3563–3568.
[43] K. Okuma, K. Hirano, C. Shioga, N. Nagahora, K. Shioji, Bull. Chem. Soc. Jpn. 86 (2013) 615–619.
[44] R. Martinez, D.J. Ramon, M. Yus, Tetrahedron. 62 (2006) 8988–9001.
[45] N.P. Buu-Ho, R. Royer, N.D. Xuosg, M.P. Jacquigiyo, J. Org. Chem. 18 (1953) 1209–1224.
[46] B. Simon, P.E. Hansen, Curr. Org. Chem. 4 (2000) 19–54.
[47] B. Bafti, H.A. Khabazzadeh, J. Chem. Sci. 126 (2014) 881–887.
[48] B. Singh, H. Lobo, G. Shankarling, Catal. Lett. 141 (2011) 178–182.